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ANESTHETICS

THEIR RELATIVE VALUES AND DANGERS

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"God bless the man who first invented sleep."

THE Trustees of the Fiske Fund, at the Annual Meeting of the Rhode Island Medical Society held at Providence, June 4, 1931, announced that they had awarded a premium of two hundred dollars to Albert H. Miller, M.D., of Providence, Rhode Island, for an Essay entitled "Anesthetics — Their Relative Values and Dangers."

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The spelling "anesthesia" is authorized by good usage and by the majority of the dictionaries.

ANESTHETICS . . . THEIR RELATIVE VALUES AND DANGERS

INTRODUCTION

AN anesthetic is an agent under the influence of which a person is enabled to undergo a painful operation without perception of pain. Administration of an efficient general anesthetic should result in unconsciousness, muscular relaxation and diminution in reflex activity. In the following formula, D represents the dosage of the anesthetic agent; P, the idiosyncrasy of the patient; O, the stimulation or trauma of the operation; Z, the zone or depth of anesthesia; and X, the efficiency of the anesthesia.

$$Z = D \pm P$$

$$X = \frac{Z}{O}$$

$$X = \frac{D \pm P}{O}$$

The efficiency of an anesthetic varies directly as the dosage, inversely as the operative trauma, and to a greater or less degree according to the patient's condition.

The action of anesthetics is physical rather than chemical. Their narcotic power varies as their oil-water solubility coefficient, as their power to lower surface tension and as their power to inhibit the activity of yeast which has been deprived of lipoids. When an anesthetic reaches a sufficient concentration in the tissues it paralyzes the cells but this action is reversible on lowering the concentration of the drug. In higher concentrations anesthetics produce an irreversible effect which may be fatal.

HISTORICAL BACKGROUND

Until the year 1846, the word anesthesia was not known, even the idea which the word now represents was unformulated, and that surgical operations might be performed without inflicting pain was unbelievable. In the year 1798, Dr. Thomas Beddoes, at Clifton, near Bristol, on the River Avon, had opened a Pneumatic Institution for study of the therapeutic effects of gaseous agents. From this institution, in 1800, came the

statements of the young assistant, Humphrey Davy, "as nitrous oxide in its extensive operation appears capable of destroying physical pain, it may probably be used with advantage during surgical operations in which no great effusion of blood takes place," and "modification of the powers of nitrous oxide by mixture of this gas with oxygen or common air, will probably enable the most delicately sensible to respire it without danger, and even with pleasurable effects." Then Michael Faraday, third in the chain, found that "the vapor of ether, when mixed with air, produces effects very similar to those occasioned by nitrous oxide."

This work of Beddoes, Davy and Faraday, although promising unlimited success in the relief of human suffering, was un-noted for more than a quarter of a century. During this period the operating room continued to be a chamber of horrors. Dentistry was torment. To avoid the pain of extraction it was customary to fit artifical teeth over decaying roots. Surgical operations were performed only when unavoidable and then with a technic subordinated to the necessity for avoiding prolonged suffering.

In the year 1846, anesthesia burst forth like a thunder bolt. A young dentist of Boston, William T. G. Morton, using ether, demonstrated at the Massachusetts General Hospital on the 16th of October, relief of pain during surgical operations. Leading up to this event were the studies of Charles T. Jackson, a Boston chemist, familiar with the work of Davy and Faraday; the unsuccessful attempt of Horace Wells to demonstrate anesthesia with nitrous oxide; and some years of study and experiment by Morton. He realized, as far as was humanly possible, the grandeur of his discovery and devoted his life and fortune to its development.

Anesthesia was not uniformly successful. At the eighteenth administration, the patient, Thomas Hebert, died during an operation for stone. Soon after, Ann Parkinson failed to recover from the effects of ether administered for removal of a tumor of the thigh. These deaths brought forward the question of the safety of anesthetics, a problem which today is of first importance in the consideration of their value. Searching for an agent which might be safer than ether, James Simpson introduced chloroform. The death of his patient, Hannah Greener, in January, 1848, under the influence of chloroform, brought into question the safety of this agent. From that time to the present, a constant search has been made for an ideal anesthetic but of all the agents which have been proposed, none has succeeded in displacing ether, used by Morton at his demonstration in 1846.

In 1863, Colton formed an association of dentists in New York City for the purpose of encouraging the use of nitrous oxide in dental operations and was so successful that, three years later, he was able to report a series of 20,000 cases done without accident. Nitrous oxide was available only for the briefest operations until, in 1868, Andrews, in Chicago, put into operation Davy's suggestion that nitrous oxide be mixed with oxygen, thus introducing nitrous oxide oxygen anesthesia. In 1876, Clover devised an inhaler for use with nitrous oxide and ether and originated the gas-ether sequence. In 1884, Karl Koller introduced cocaine, the main alkaloid of the coca plant, with the property of producing a localized anesthesia in the area where it is injected. A year later, Corning accidentally introduced cocaine into the epidural canal and thus discovered spinal anesthesia. Ethyl chloride was used by Richardson in 1867, but did not come into extensive use until a Swiss surgeon, in 1896, reported 2,500 satisfactory cases. In 1905, Braun introduced novocaine, a synthetic substitute for cocaine, with the advantage of less toxic action. In 1917, Cotton described the advantages of ethylene as a general anesthetic. In 1923, Luckhardt and Carter reported the first 106 cases of ethylene anesthesia from the Presbyterian Hospital in Chicago.

THE VARIOUS ANESTHETICS

In his monumental "List of Anesthetics," Baskerville[101] catalogued more than four hundred drugs which have been found to have anesthetic properties. Most of these have survived for a day and then been abandoned.

Anesthetic agents in practical use at the present time are:

1. Gases:—Nitrous oxide, ethylene, carbon dioxide.
2. Liquids:—Ether, chloroform, ethyl chloride.
3. Solids:—Cocaine, procaine, hypnotics used as anesthetics.

The methods by which anesthetics may be administered are:

Inhalation, insufflation, oral, rectal, intravenous, hypodermatic, intramuscular, intraspinal, by application to mucous membranes.

From their effects, anesthetic agents are characterized as:

General: Affecting the entire organism and destroying consciousness.

Regional: Affecting some part of the organism and not necessarily interfering with consciousness. All regional anesthetics have some general action.

THE GASEOUS ANESTHETICS

NITROUS OXIDE

Preparation: On heating ammonium nitrate in a retort, it first liquefies and then breaks up into nitrous oxide and water.

$$\underset{\text{ammonium nitrate}}{NH_4NO_3} = \underset{\text{nitrous oxide}}{N_2O} + \underset{\text{water}}{2H_2O}$$

Ammonium nitrate, in quantities of 40 pounds at a time, is put into two aluminum retorts and heated to 400°C. Nitrous oxide and water result. After passing through condensing coils where the water is removed, the gas passes through wash bottles containing potassium permanganate to remove oxides, through a tower containing coke upon which sodium hydrate solution is sprayed to remove nitric acid, through wash bottles containing sulphuric acid to remove free akalies, through fresh water, and then accumulates in a gasometer. The gas is compressed and stored in steel cylinders. During compression, the gas is dehydrated mechanically and by the action of calcium chloride or other efficient drying agents. In the cylinders, the dry gas is held as a clear, mobile liquid, at a pressure of 1500 pounds to the square inch.

Properties: Nitrous oxide is a colorless gas with a faint and not unpleasant musty odor. It is heavier than air, having a specific gravity of 1.527. Four gallons of the gas weigh one ounce. Compressed to a liquid, nitrous oxide is not readily decomposed and keeps indefinitely. The gas supports combustion. Mixtures of nitrous oxide and oxygen are not explosive in any concentration.

Physiological Effects: Nitrous oxide is not irritating to the respiratory mucous membranes. Although it contains a greater proportion of oxygen than is present in the atmosphere, the oxygen is in such stable combination that it is not available for the requirements of respiration. When pure nitrous oxide is inhaled, the respiratory center is rapidly paralyzed from anoxemia, the respiration becoming first rapid and deep, then slow and shallow, and finally ceasing altogether. Anesthesia is induced within thirty seconds. When sufficient oxygen to avoid asphyxial symptoms is added to nitrous oxide, anesthesia may be indefinitely prolonged. Induction is not objectionable to the patient and recovery results immediately after the administration has been discontinued. The patient recovering from nitrous oxide oxygen anesthesia often notes that he has awakened from a dream, the substance of which he has for-

gotten. Occasionally one complains that, while he has felt no pain, he has not completely lost consciousness.

The amount of oxygen compatible with satisfactory nitrous oxide oxygen anesthesia is usually 8 to 10 per cent, but must be modified to suit the patient's condition. One suffering from profound anemia or in a condition of shock may exhibit deep anesthesia on a 50 per cent mixture, while to secure satisfactory anesthesia for highly nervous patients or those of plethoric type, registering a high blood pressure, it is often necessary to cut down the oxygen percentage to such an extent that a severe, sometimes fatal anoxemia may result. When sufficient oxygen to supply the respiratory need is added, active reflexes and muscular rigidity may persist, rendering anesthesia insufficient for severe surgical procedures. Early signs of oxygen deficiency are reflex activity, muscular rigidity, cyanosis, excessive perspiration and an increase in blood pressure.

In the tissues, nitrous oxide is held in solution and not in chemical combination. The entire amount administered is eliminated unchanged. Elimination is completed within two minutes after administration has been discontinued. With sufficient oxygen, nitrous oxide has little effect on blood pressure, heart, lungs, liver or kidneys. It is not prone to cause acidosis. Blood sugar is only slightly changed. Metabolism and the phagocytic power of the blood are only transiently disturbed. Peristalsis is increased with a tendency to irregularity in the contractions. On recovery, peristalsis is inhibited for about an hour.

Advantages of nitrous oxide oxygen anesthesia:

Comfortable induction.
Limitation of the actual duration of anesthesia to the shortest possible time.
Short period of fasting and deprivation of fluids.
Immediate recovery of consciousness.
Lack of interference with body functions.
Absence of respiratory and renal irritation.

Disadvantages of nitrous oxide oxygen anesthesia:

Lack of relaxation.
Liability to anoxemia.

To overcome the disadvantages of nitrous oxide oxygen anesthesia, it is customary to reinforce the anesthetic by adding ether vapor to the mixture. It is doubted that the results of anesthesia with nitrous oxide oxygen ether are often better than could be obtained by the careful use of ether alone. Even with the aid of preliminary drugging and the

addition of ether, the most expert administrator may fail to secure satisfactory anesthesia with nitrous oxide oxygen. Deaths attributed to nitrous oxide oxygen are generally caused by anoxemia, due to insufficient oxygen in the mixture, or to respiratory spasm which prevents oxygen from gaining admittance to the pulmonary alveoli.

ETHYLENE

Preparation: Ethylene results from dehydration of alcohol or from cracking a carbohydrate.

C_2H_5OH	=	C_2H_4	+	H_2O
alcohol		ethylene		water

A molecule of water may be removed from alcohol by the action of hot sulphuric acid, orthophosphoric acid or kaolin. Alcohol is introduced slowly into a generating flask containing one of these agents kept at a temperature of 210° to 230°C. The resulting ethylene gas, with a mixture of water vapor, passes through a condenser to remove the water, through wash bottles containing potassium hydroxide to remove carbon dioxide, and is collected in a gasometer. For storage and transportation, the gas is compressed into steel cylinders.

Properties: Ethylene is a colorless gas with a slightly pungent and rather foul odor. It is a little lighter than atmospheric air, having a specific gravity of .978. With this specific gravity, so nearly identical with that of the atmosphere, it diffuses rapidly in all directions. Ethylene burns with a luminous flame. The pure gas stored in cylinders is not explosive, but if oxygen, either pure or in combination, gains entrance to a cylinder, an explosive mixture may result and the cylinder be shattered. A mixture of ethylene with oxygen, 5 to 70 per cent is explosive. The greatest hazard is from a mixture containing 25 per cent ethylene with 75 per cent oxygen. This mixture detonates with great force, the explosive wave travelling with extreme rapidity and passing through a fine wire screen without interruption. The mixture is readily exploded by an open flame, a heated cautery or an electric spark. Characteristic ethylene explosions occur when least expected, often in the practice of experts when all known precautions have been taken.

Physiological Effects: Inhalation of a mixture of ethylene with 10 to 20 per cent oxygen produces general anesthesia. These percentages of oxygen more nearly fulfill the body requirements than do the amounts permitted with nitrous oxide. For this reason, ethylene is a more efficient anesthetic than nitrous oxide and provides efficient anesthesia for

most operations, with sufficient oxygen to prevent anoxemia. In some instances satisfactory anesthesia cannot be secured without cutting down the oxygen percentage to a dangerous level. Symptoms of oxygen deficiency comparable to those noted with nitrous oxide oxygen then develop.

Administered with sufficient oxygen, ethylene has little effect on blood pressure, heart, lungs, liver or kidneys. No irritation of the respiratory mucous membrane results. There is a slight and transitory tendency to the production of acidosis. Blood sugar is somewhat increased. Coagulation time is unaffected. Peristalsis is well maintained during operation and recovery. Ethylene has less effect in inhibiting uterine contractions than any other anesthetic. The entire amount administered is eliminated. Elimination is rapid but somewhat slower than in the case of nitrous oxide.

Advantages of ethylene oxygen anesthesia:

In comparison with nitrous oxide oxygen:

More efficient anesthesia.
Better relaxation.
Less tendency to anoxemia and its attendant symptoms.

In general:

Ease of induction.
Limitation of the actual duration of anesthesia.
Lack of interference with body functions.
Lack of excessive perspiration and secretion of mucus.
Absence of respiratory or renal irritation.
Rapid recovery of consciousness.
Diminution of post-operative discomfort.

Disadvantages of ethylene oxygen anesthesia:

The persistent and generally objectionable odor.
Difficulty in obtaining relaxation.
Liability to anoxemia.
Danger of explosion.

To secure the desired degree of relaxation in cases when ethylene oxygen is inefficient, it is customary to reinforce anesthesia by the addition of ether vapor to the mixture. As with nitrous oxide oxygen, this technic is of doubtful advantage. Fatalities under ethylene oxygen, other than those caused by explosions, are generally due to anoxemia.

CARBON DIOXIDE

Preparation: Carbon dioxide is produced by the interaction of a carbonate and an acid.

$CaCO_3$	+	2HCl	=	CO_2	+	$CaCl_2$	+	H_2O
calcium carbonate		hydrochloric acid		carbon dioxide		calcium chloride		water

Carbon dioxide is widely distributed in nature. It is the main product of combustion, of the respiration of animals, and of decay. Pure atmospheric air contains .03 per cent carbon dioxide. Commercial carbon dioxide is supplied in cylinders, in which it is compressed to a liquid.

Properties: Carbon dioxide is a colorless gas having a slightly acid odor and taste. It will not support combustion and is not explosive. It is heavier than air with a specific gravity of 1.977.

Physiological Effects: The respiratory center is very sensitive to changes in the carbon dioxide tension of the arterial blood. The volume of carbon dioxide in the alveolar air is about 5 per cent. An increase of .2 per cent will double the volume of respiration. A diminution of .2 per cent will produce apnea. The percentage of carbon dioxide in the alveolar air and in the arterial blood is kept constant by the action of the respiratory center. A slight increase in the arterial carbon dioxide stimulates the respiratory center, increases the volume of respiration, and results in excretion of the excess carbon dioxide and return of the percentage to normal. This mechanism is the first outpost against the development of acidosis. The use of carbon dioxide in anesthesia must interfere more or less with this mechanism. When carbon dioxide is added to anesthetic mixtures or when it accumulates in any method utilizing rebreathing, the acid base balance is interfered with.

Carbon dioxide is not irritant to the respiratory mucous membrane. Thirty per cent carbon dioxide in oxygen causes an uncomfortable feeling of not being able to catch the breath but more dilute mixtures are pleasant to inhale. Inhalation of pure carbon dioxide causes a rapid rise in blood pressure, slowing of the pulse and stimulation of the respiration. The blood pressure, at first increased, soon falls, the action of the heart and respiration ceases and death results. Inhalation of 30 per cent carbon dioxide in oxygen rapidly induces general anesthesia. The muscles are relaxed, the respiration is deep but not rapid, the pulse rate is increased during induction but is reduced during the subsequent anesthesia. The blood pressure is raised to a high point during induction but soon drops to the normal level. Anesthesia is complete in one to

two minutes. A smooth and pleasant induction for ether anesthesia is thus obtained.

Inhalation of 5 to 10 per cent mixtures of carbon dioxide in oxygen are used to assist in inducing anesthesia, to hasten recovery from the influence of anesthetics and to temporarily raise the blood pressure. The anesthetic property of carbon dioxide is utilized in all methods of general anesthesia in which rebreathing is employed. If 1 to 5 per cent of the nitrous oxide in a nitrous oxide oxygen mixture is replaced with carbon dioxide, anesthesia is deepened not only from the anesthetic property of carbon dioxide but also from its effect in stimulating the respiratory center, thus rendering a larger surface of the respiratory mucous membrane available for absorption of the anesthetic. When the administration has been discontinued, the effect of a small proportion of carbon dioxide is to hasten the elimination of the anesthetic through stimulation of the respiration.

THE LIQUID ANESTHETIC AGENTS

ETHER

Preparation: Ethyl or sulphuric ether results from distillation of a mixture of ethyl alcohol and sulphuric acid.

$2C_2H_6O$	+	H_2SO_4	=	$C_4H_{10}O$	+	H_2O	+	H_2SO_4
alcohol		sulphuric acid		ether		water		sulphuric acid

As the sulphuric acid is unaffected, the process is made continuous by arranging a constant flow of alcohol into the still. Five parts of 90 per cent alcohol and nine parts of concentrated sulphuric acid and placed in a still and heated to the boiling point, 140°C. Alcohol is allowed to flow constantly into the still at a rate such that the temperature remains nearly constant. The distillate, containing ether, alcohol, water and sulphur dioxide, passes through an acid trap containing sodium hydrate, and a scrubber, where most of the alcohol is removed by agitation with a small amount of water. The ether vapor is dried over calcium chloride and is finally condensed to liquid ether. Pure ether for anesthesia is sealed in air tight bottles or cans, with painstaking precautions against contamination.

Properties: Ether is a clear, very mobile liquid with a pungent, penetrating odor and a burning taste. It is soluble in about ten times its volume of water. The specific gravity of the liquid is .716. A half

pound can should contain 11.17 fluid ounces. Under atmospheric pressure, liquid ether boils at 35.5° C. (96° F.), forming a vapor of specific gravity, 2.586. Vaporizing under these conditions, ether expands in volume 303 times. A liter of pure ether vapor weighs 3.30365 grams. As it is 2.586 times as heavy as air, ether vapor sinks to the bottom of a vessel or to the floor of the room in which it may be liberated.

Ether vaporizes readily at all temperatures, the rate of vaporization depending upon the temperature of the liquid, the extent of the evaporating surface, the rate of renewal of the atmosphere, and inversely as the degree of saturation of the atmosphere. The temperature of the vapor is identical with that of the liquid. As ether vaporizes, the liquid ether remaining becomes constantly colder and the rate of evaporation constantly diminishes. The degree to which the atmosphere can be saturated with ether vapor depends upon the temperature.

MAXIMUM SATURATION WITH ETHER VAPOR

Temperature		Tension mm. Hg.	Volume Per cent
Cent.	Fah.		
0.	32	182.3	23.2
10.	50	286.5	37.7
20.	68	434.8	57.2
30.	86	637.	83.7
35.5	96	760.	100.

Three units of measurement are in use for indicating the strength of ether vapor used in anesthesia: percentage by weight, percentage by volume, and ether vapor tension in millimeters of mercury.

Weight per cent	Volume per cent	Vapor tension
10.	4.11	31.24
15.	6.38	48.5
20.	8.82	67.03
30.	14.20	107.9
40.	20.44	155.5
50.	27.92	212.2

Ether burns with a luminous flame. The vapor forms an explosive mixture when mixed with air or oxygen. The mixture may be exploded by an open flame, a heated cautery or an electric spark. Such explosions occur rarely. Differing from light, readily diffusible ethylene, the heavy, concrete ether vapor sinks rapidly to the floor. Only after hours of administration in a small, unventilated room does the concentration of ether vapor become sufficient to form an explosive mixture. Explosions

of ether vapor are the result of gross negligence. Such have occurred as the result of placing a cone charged with ether on top of a sparkling electric motor or operating a heated cautery blade in the mouth of an etherized patient.

Physiological Effects: Ether is administered as a general anesthetic by inhalation, by insufflation, by mouth, by rectum, and intravenously. Pure ether vapor is difficult to obtain, is irrespirable, and is never used in anesthesia. A 15 per cent by weight ether vapor is sufficient for induction and maintenance of anesthesia but with this concentration the period of induction is greatly prolonged. Temporary use of a 40 per cent by weight vapor shortens the induction period to from eight to twelve minutes. Stronger concentrations may displace so much atmospheric oxygen that signs of anoxemia develop. Providing the oxygen supply be sufficient, the color of a patient under ether anesthesia is slightly heightened. Cyanosis indicates interference with the supply of oxygen either from overdosage or from mechanical interference with the respiratory mechanism. In satisfactory etherization, cyanosis never occurs.

The entire amount of ether administered is eliminated unchanged. One-half the entire amount is eliminated within the first five minutes, most of the remainder, within forty-five minutes, and the whole amount in seven to eight hours.

Liquid ether allowed to evaporate on the skin produces a sensation of cold and some local anesthesia. If the vapor is confined, it causes irritation and may produce a blister. Etherization is accompanied by dilatation of the superficial blood vessels and some perspiration, the amount depending upon the dosage employed. A bright, macular erythema often appears upon the chest during induction and persists for about twenty minutes. Less frequently, this eruption involves the skin of the abdomen and extremities.

The effect upon the conjunctiva resembles that upon the skin. Liquid ether may be poured into the eye with little effect. If the eyes are covered so that the vapor is confined, a severe conjunctivitis results. Secretion of tears is stimulated during etherization to a degree depending upon the dosage.

Ether vapor is irritant to the respiratory mucous membrane, the effect depending upon the concentration of the vapor. A concentrated vapor causes a profuse secretion of mucus. Overconcentration during induction may cause coughing, a sense of suffocation, and temporary cessation of respiration.

During etherization, the respiratory movements are increased in depth and frequency. If an overdose is administered, respiration becomes shallow and feeble. Periodic respiration may develop and respiration may cease altogether.

Ether is a powerful cardiac stimulant, increasing the force and frequency of the heart beats. An overdose may result in secondary circulatory depression. By careful attention to proper dosage, it is frequently possible to administer ether for a long operation, without perceptible effect on the rate or quality of the pulse.

The presence of ether in the blood results in leucocytosis and a transient destruction of red blood cells. Increase in blood sugar, sometimes amounting to 73 per cent, can be controlled by the use of insulin. Acidosis usually transitory, regularly accompanies etherization.

The blood pressure is little affected by the administration of ether in proper dosage, provided the supply of oxygen be sufficient. An increase in blood pressure accompanies anoxemia. With respiratory obstruction, the systolic pressure may be increased twenty millimeters. Overdosage with ether results in symptoms associated with surgical shock: profound prostration of body functions, cold and moist skin, dilated pupils, ashy color, small, usually rapid pulse, superficial respiration, sometimes irregular and halting, and a low blood pressure with pulse pressure affected out of proportion to the diastolic pressure.

Under deep etherization, the muscles are relaxed. Lack of relaxation is due to incomplete saturation of the tissues or to the presence of anoxemia. If anoxemia develops, the muscular system is thrown into a state of tonic contraction. Spasm of the muscles of the jaw and of respiration halt the respiratory movements and form a vicious cycle with production of increasing anoxemia.

The glandular secretions are stimulated by ether. Secretion of mucus in the upper air passages, trachea, and bronchial tubes is increased to a degree depending upon the dosage employed. A toxic thyroid may be so over-stimulated that death results.

The renal secretion is first stimulated and then depressed. Transient albuminuria frequently follows etherization. With nephritis present, urinary suppression and death in coma may result. Stimulation of the sugar forming function of the liver results in hyperglycemia. Acetone and diacetic acid are frequently present in the urine.

Peristalsis in the stomach, small intestines and colon is abolished during etherization but rapidly returns on recovery, with an increased degree of activity.

Metabolism steadily diminishes as etherization progresses.

The nervous centers are at first stimulated and then depressed. Perception of pain disappears early. Sight, smell and hearing are lost. Hearing is the last to disappear and the first to return. Memory is lost early and returns some time after consciousness has apparently been established.

The reflexes are lost or diminished. Loss of lid reflex and of the pupillary reflex are used as signs of sufficient anesthesia. Persistence of the sneezing, coughing or swallowing reflexes denote a light zone of anesthesia.

Advantages of Ether Anesthesia:

Efficiency: Fewer failures to secure satisfactory anesthesia occur with ether than in the case of any other agent. Ether is the anesthetic chosen to fortify nitrous oxide oxygen or ethylene oxygen and often to supplement other agents when these prove inefficient in securing satisfactory results.

Adaptability: Ether is used by various inhalation methods and by intravenous and rectal routes.

Safety: Any other anesthetic agent, used in the careless manner which has characterized the administration of ether, would have resulted in so many fatalities that its use would long since have been abandoned.

Disadvantages of Ether Anesthesia:

Unpleasant Odor of the Vapor: This objection has been overcome during induction by preceding the administration of ether by nitrous oxide.

Unpleasant odor and taste noted during recovery.

Irritant effect on the kidneys and on the respiratory mucous membrane.

Tendency to result in nausea, vomiting, and acidosis.

It is unlikely that death ever results from proper administration of ether to healthy subjects. When an overdose has been employed, death may result from respiratory paralysis. In deep concentration, the irritating effect of ether vapor may cause respiratory spasm and severe and possibly fatal anoxemia. Irritation of the respiratory mucous membrane may produce a profuse secretion of mucus which interferes seriously with respiration. Administration by inhalation may light up a quiescent pulmonary tuberculosis. Pulmonary complications follow

etherization but not more frequently than after other anesthetic agents. Renal irritation following etherization may result fatally in victims of nephritis. In traumatic shock, administration of ether may accentuate the symptoms and hasten the fatality.

CHLOROFORM

Preparation: Chloroform is prepared by the action of chlorinated lime upon alcohol.

$8Ca(OCl)_2$	+	$3C_2H_6O$	=	$2CHCl_3$	+	$3CaCO_3$	+	
chlorinated lime		alcohol		chloroform		calcium carbonate		
$5CaCl_2$	+	$6H_2O$	+	CO_2				
calcium chloride		water		carbon dioxide				

Chloroform is preserved by the addition of 1 per cent. alcohol and is stored in colored glass bottles.

Properties: Chloroform is a colorless, volatile liquid with a pleasing odor and a burning taste. The specific gravity of the liquid is 1.486 and of the vapor is 4.20. It boils at 60° C. (140° F.). Chloroform is not inflammable. Mixtures of the vapor with air or oxygen in any concentration are not explosive. Exposed to light, chloroform slowly decomposes. In the presence of an open flame, the vapor oxidizes with formation of phosgene gas, a powerful irritant to mucous membranes, causing an irritant cough and conjunctival irritation.

Physiological Effects: Chloroform is a powerful general anesthetic. It is efficient in producing muscular relaxation and in abolishing reflexes. A concentration of 5 per cent. of the vapor in air rapidly induces anesthesia. A concentration of 1 per cent. by volume suffices for maintenance.

Liquid chloroform applied to skin or mucous membrane is a powerful irritant.

Inhalation of concentrated chloroform vapor may produce laryngeal spasm and block respiratory movements. The dilute vapor used for anesthesia is unirritating to mucous membranes. Secretion of mucus, at first stimulated, is later diminished. The respiration is slow, full and regular but, with overdosage, becomes shallow and irregular.

Chloroform is a direct heart depressor, slight overdosage resulting in paralysis of the cardiac muscle and cardiac dilatation. The danger of

cardiac paralysis results from oversaturation of the blood passing through the coronary arteries at some one time rather than from oversaturation of the tissues in general. For this reason, chloroform should never be intermittently administered, but any increase in dosage should be gradually effected. The pulse should be full and steady. Any change in the rhythm or quality is a sign of danger. The blood pressure is generally lowered during chloroform anesthesia.

Muscular spasm may occur during induction with chloroform. The muscles are relaxed during complete anesthesia.

The urinary secretion is first stimulated and then diminished. Albuminuria is frequently encountered after chloroform anesthesia. The hepatic cells are so affected that metabolism of fats is depressed. Prolonged or repeated administration of chloroform is likely to produce a fatty degeneration of the liver, kidneys and the heart. This results in the condition known as delayed chloroform poisoning, developing about twenty-four hours after the termination of anesthesia, appearing most often in children, and often terminating in death.

The rate of elimination of chloroform corresponds with that of ether. As it is broken down in the tissues, the entire amount administered cannot be recovered.

Advantages of chloroform anesthesia:

The pleasant odor.
Small bulk of the agent required.
Lack of respiratory irritation.
Complete muscular relaxation.
Freedom from danger of fire or explosion.

Disadvantages of chloroform anesthesia:

Danger of fatality from direct cardiac paralysis, indirect effect on the heart or the medullary centers, or secondary toxic effect on the liver, kidneys and heart.

Deaths ascribed to chloroform occur during induction, during the later stages of prolonged administration, or several days after the operation. The deaths which occur during induction come suddenly, without premonitory symptoms. The patient has shown signs of incomplete anesthesia, the administrator applies an increased amount of chloroform, and the heart action ceases while respiration continues for some seconds. These deaths, often attributed to status lymphaticus, are more probably due to the effect on the heart muscle of a momentary over-

dosage of the anesthetic. The same effect may be produced by a deep inhalation of concentrated chloroform vapor after holding the breath.

Deaths occurring later in the administration result from the toxic effect of the drug upon the heart muscle, from vasomotor depression, or from depression of the respiratory center. A number of deaths have occurred during administration of chloroform to patients in the sitting posture. This position favors the development of cardiac syncope and should never be used when chloroform is administered. The symptoms of delayed chloroform poisoning are those of an acute acidosis. Fatty degeneration of the liver, kidneys and heart are found at postmortem examination.

The Committee on Anesthesia of the American Medical Association, in 1912, reported that:

> "The use of chloroform as the anesthetic for major operations is no longer justifiable.
>
> "For minor operations also the use of chloroform should cease.
>
> "Chloroform is sometimes found convenient for initiating anesthesia in alcoholics or other difficult subjects."

In view of this authoritative statement, chloroform can be used in this country only when definitely indicated.

ETHYL CHLORIDE

Preparation: Ethyl chloride is prepared by the action of hydrochloric acid on ethyl alcohol.

HCl	+	C_2H_6O	=	C_2H_5Cl	+	H_2O
hydrochloric acid		alcohol		ethyl chloride		water

Hydrochloric gas is passed into alcohol. After allowing the solution to set for some time, it is distilled on a water bath with the production of ethyl chloride. If zinc chloride is added to the solution, the entire amount of alcohol may be converted. Ethyl chloride is stored in clear glass containers sealed with air tight valves, or in sealed glass ampoules.

Properties: Ethyl chloride is a colorless, mobile liquid, having a sweet, agreeable odor and a burning taste. It boils at 13° C. (55.4° F.) and vaporizes immediately on liberation from its container at room

temperature. Ethyl chloride is very inflammable and cannot be safely used in proximity to an open flame. On evaporation it causes intense cold, a property made use of in securing local anesthesia by freezing the tissues.

Physiological Effects: Inhalation of a dilute mixture of ethyl chloride vapor with air or oxygen rapidly induces general anesthesia.

Ethyl chloride is not irritating to mucous membranes. It does not cause respiratory irritation and may be sprayed upon the conjunctiva without serious results. The respiratory movements are increased in depth and frequency. Stertorous breathing appears early in the administration. Overdosage results in respiratory failure but this is secondary to circulatory depression with failure of the blood supply to the respiratory center. Like chloroform, ethyl chloride has an immediate toxic effect upon the heart and a momentary overdosage may be fatal. There is a uniform fall in blood pressure due to cardiac inhibition. In case of overdosage, the fall in blood pressure is rapid and accompanied by symptoms of syncope.

It may be impossible to secure muscular relaxation with ethyl chloride without administering a dangerous dose. During induction, muscular rigidity is often noted.

Ethyl chloride is rapidly absorbed and as rapidly eliminated, the entire amount being eliminated within five minutes from the close of anesthesia. Excretion takes place through the lungs. The liver and kidneys are little affected. Nausea and vomiting are not likely to result.

Advantages of ethyl chloride anesthesia:

Rapid, pleasant induction.
Freedom from after effects.

Disadvantages of ethyl chloride anesthesia:

Lack of muscular relaxation.
Liability to fatal syncope.

The principal use of ethyl chloride has been to secure an agreeable induction for ether anesthesia. For this purpose, nitrous oxide is nearly as efficient and far safer.

ANESTHETIC AGENTS—SOLIDS

COCAINE

Source: Cocaine is an alkaloid obtained from the leaves of Erythoxylon coca, a plant native to tropical South America.

Properties: Cocaine occurs as a white powder, consisting of large, colorless crystals. It has a bitter taste and causes temporary numbness of tongue. Because of its comparative insolubility, six hundred parts of water being required for solution, the more soluble hydrochloride is used. Cocaine hydrochloride is a white, crystalline powder which is soluble in .4 parts water at 25° C. (77° F.). The solution may be sterilized at 80° C. for an hour, on three successive days but is decomposed by prolonged boiling.

Physiological Effects: Cocaine produces a selective, temporary paralysis of sensory nerves and nerve endings. Applied to mucous membranes, it immediately causes blanching of the membranes. It is readily absorbed through mucous membranes and produces anesthesia by its effects on the nerve endings. Injected beneath the skin, cocaine produces transient paralysis of the sensory endings in the region injected. The sensation of pain disappears before that of touch but with sufficient concentration, all nerve endings are paralyzed. Applied to nerve trunks or injected in their neighborhood, cocaine paraylzes the sensory fibers and produces anesthesia in the parts which they supply. Motor paraylsis may result but comes later than the sensory effect.

In addition to its regional action, cocaine has important general effects. The higher centers of the brain are powerfully stimulated, resulting in mental exhilaration, wakefulness and greater power to endure hunger and fatigue. The pulse is increased in force and frequency, the respiration is stimulated and the kidney output is increased. From stimulation of the sympathetic nerve endings, vaso-constriction results and the pupils become dilated.

The maximum safe dose of cocaine for subcutaneous use is stated to be one grain. The toxic effects are extremely irregular, depending upon the rate at which the drug has been absorbed and upon the individual susceptibility of the patient. A mild reaction is characterized by pallor, sweating, dilated pupils and a drop in the pulse rate. These symptoms are more likely to develop if the patient is in the sitting posture. Cyanosis, nausea and vomiting and unconsciousness may follow. In the more severe cases of cocaine poisoning, clonic convulsions, unconsciousness

and collapse occur in rapid succession and death results from respiratory depression.

Because of the danger attending the use of cocaine, it has been entirely discarded except for operations about the eye, nose and throat. The mucous membrane of the eye and nose can be anesthetized by the external application of cocaine hydrochloride with very little danger. For removal of tonsils, hypodermic use of one half to one per cent. cocaine solution with the addition of epinephrin solution, ten to fifteen minims per ounce, is still recommended.

Frequent occurrence of toxic effects from cocaine have led to a search for other agents capable of producing regional anesthesia but lacking the toxic properties of cocaine. Among the cocaine substitutes are butyn, alypin, tropococaine, apothesine, B-eucaine, stovaine, novocaine, and nupercaine. Novocaine, from its tried efficiency and comparative safety, is the most popular of these agents.

NOVOCAINE

Occurrence: The American product, procaine, and the French, neocaine, are chemically identical with novocaine. They are derivitives of benzoic acid and contain an amido group. Novocaine occurs as a white, crystalline powder, freely soluble in water and soluble in its own weight of spinal fluid. The solution does not decompose on boiling and may safely be heated to 120° C. (248° F.). Utilizing its vaso-constrictor action, epinephrin is often added to novocaine solutions in order to impede the diffusion of the novocaine and limit the area of anesthesia. The solution for subcutaneous use, usually one half to one per cent., is prepared by dissolving novocaine tablets in sterile, distilled water and is sterilized by heating in an autoclave at fifteen pounds steam pressure. Epinephrin, four to six drops of the one to 1,000 solution per ounce, is added to the novocaine solution shortly before its use is required. Novocaine is also available sterilized in sealed ampoules; an example is the ampoule containing novocaine, .02 Gram, epinephrin, .00004 gram, sodium chloride, .009 gram, potassium sulphate, .008 gram, and distilled water to 2 cc. This ampoule contains 2 cc. of one per cent. novocaine.

For intra-spinal injection, novocaine may be dissolved in sterile distilled water, in saline solution, or in spinal fluid. Alcohol may be added to lower the specific gravity or glucose to increase the specific gravity of the solution. Spinocaine is a solution of novocaine in normal saline with the addition of strychnine sulphate, alcohol, and starch paste.

Physiological Effects: Novocaine has practically no power of penetration and cannot replace cocaine for regional anesthesia of mucous membranes. For terminal or conduction anesthesia, novocaine is an efficient substitute. Subcutaneous injection of one half to one per cent, novocaine solution rapidly induces anesthesia in the region injected. The effect begins to wear away after fifteen minutes but if epinephrin has been added to the solution, anesthesia may persist for one to three hours. Injection within a nerve sheath immediately produces anesthesia of the distribution area of the nerve. Injection in the vicinity of a nerve trunk produces a similar effect, but fifteen to twenty minutes may elapse before the maximum effect is obtained. Injected into the subarachnoid space, novocaine produces anesthesia, at first affecting the perineum and the feet and then spreading up the legs and body to its upper limit.

Novocaine solutions are somewhat irritating to mucous membranes and to the skin. Repeated use may cause dermatitis. Subcutaneous injection of novocaine solution has been followed by sloughing but this effect is more likely due to the epinephrin in the solution than to novocaine.

Novocaine is somewhat irritating to the kidneys and its use may be followed by albuminuria. It is rapidly broken down in the liver and is excreted in inert form. No trace of novocaine can be recovered from the urine. The comparative safety of novocaine results from the slowness with which it is absorbed and upon its rapid destruction in the liver. Injected into a vein, the toxicity of novocaine is greatly increased. When injected subcutaneously, its toxicity is one tenth that of cocaine but injected into a vein, novocaine has more than five times the toxicity resulting from subcutaneous administration. Because of its rapid destruction in the liver, novocaine has no cumulative effect.

During induction, the pulse rate is usually increased but soon returns to its accustomed frequency. The blood pressure may be unaffected but frequently falls fifteen to twenty millimeters.

In overdose, novocaine produces convulsions, unconsciousness, and death from respiratory failure. A milder reaction is characterized by a fall in the pulse rate, faintness, pallor and sweating. Toxic effects from novocaine depend upon the amount injected and upon the rate at which the drug is injected and absorbed. Susceptibility to the effects of the drug may be encountered, especially among patients suffering from uncompensated cardiac weakness. Unexpected ill effects from comparatively small amounts of novocaine follow accidental puncture and entrance of a vein.

HYPNOTICS USED AS ANESTHETICS

In classifying hypnotic agents, it is found that the pure hypnotics have no other effect, in therapeutic dosage, than to produce sleep. Others, in addition to their hypnotic action, have a powerful sedative effect on conditions of motor excitation and still others show such a powerful action in relief of pain that the analgesic action overshadows the hypnotic effect. All of these agents, in sufficient dosage, will produce complete anesthesia. Some of the hypnotics have been exploited for a time as proper anesthetic agents but have been retired, as the result of experience, to the position of valuable adjuncts to the safer and more efficient anesthetics. The hypnotics are classified as:[102]

Alcohols,
Aldehydes,
Halogens,
The sulphone group,
The ureide group,
    Derivitives of urea,
    Derivitives of urethane,
Opium alkaloids,
Hyoscin.

ALCOHOLS

Avertine

Tribromethanol, or avertine, is a white, crystalline powder, prepared by reduction of bromal hydrate by alcohol in the presence of ethoxide. It is soluble in water at 40° C. (104° F.) to 3.5 per cent. At 70° C. (158° F.), the solution decomposes with formation of hydrobromic acid and dibromacetaldehyde. At room temperature, it decomposes slowly. The solution must be freshly prepared and immediately before being used, should be tested for acidity with a .1 per cent solution of congo red. If the test shows a blue or violet color, the solution must be discarded. If the solution is allowed to cool, the avertine may crystallize out. The avertine solution, then, must be freshly prepared, it must be neither too hot nor too cold, and it must be tested for acidity immediately before being used. Avertine is freely soluble in amylene hydrate and is available in solution containing 1 gram to each cc. of amylene hydrate. For rectal injection, a 3 per cent. solution is prepared with distilled water.

Physiological Effects: Administered as a rectal injection in a dosage of .06 to .1 cc. (60 to 100 milligrams) to a kilogram (2.2 pounds) of body weight, avertine is an efficient hypnotic. Larger doses produce complete anesthesia, but this use is accompanied with considerable danger and has resulted in a number of fatalities due to respiratory depression. Fatty degeneration of the liver and kidneys has been found post mortem. An avertine solution which has been allowed to decompose will produce erosion of the intestinal mucous membrane and may result in the death of the patient.

As a preliminary hypnotic, the solution of avertine, freshly prepared and tested, is administered by rectum a half hour before the time for operation. In about seven minutes, the patient quietly falls into a sleep which lasts for one to six hours. The effect of avertine is supplemented by nitrous oxide oxygen, ether, or the regional use of novocaine. When an inhalation anesthetic is administered, it must be used in diminished dosage and with great care.

The heart action is not affected by a hypnotic dose of avertine. The blood pressure is somewhat lowered. The rate and volume of respiration is diminished. In overdosage, avertine produces a depression of the respiratory center which is difficult to overcome and may result in fatality. The use of avertine is attended with some increase in blood sugar and a tendency to the production of acidosis. Avertine is eliminated by the kidneys.

Advantages of the use of avertine in anesthesia:

Smooth, rapid induction without excitement,
Gradual recovery after one to six hours,
Freedom from nausea and vomiting,
Freedom from excessive perspiration and excessive secretion of mucus,
Lack of memory of anything connected with the operation.

Disadvantages of avertine:

Respiratory depression,
Impairment of kidney function,
Danger resulting from disintegration of the solution.

ALDEHYDES

PARALDEHYDE

Paraldehyde is a colorless liquid with an unpleasant, penetrating odor and a disagreeable taste. In doses of 15 cc., it is a pure hypnotic. It does not depress the heart action and large amounts are required to produce respiratory depression. It acts first on the higher cerebral centers and later affects other parts of the nervous system. Paraldehyde is used in preparing the solution for ether oil colonic anesthesia.

HALOGENS

CHLORAL

Chloral hydrate is an efficient hypnotic. In large doses it produces complete anesthesia. It was the first drug used for intravenous anesthesia. Chloral causes marked depression of both heart action and respiration. Because of its inherent danger, its use in anesthesia has been abandoned.

SULPHONES

SULPHONAL, TRIONAL AND TETRONAL

These drugs are almost insoluble in water. They are slow in absorption and elimination and have a marked cumulative effect.

THE UREIDE GROUP

DERIVITIVES OF UREA

Barbituric acid, $CO(NHCO)_2CH_2$, is derived from urea, HNCO. The numerous salts derived from barbituric acid are formed by substituting various radicals for atoms of hydrogen. The sodium salts are generally preferable because of their greater solubility. Solutions of barbiturates are not stable and must be freshly prepared. The salt known as barbital (barbitone, veronal) is di-ethyl barbiturate. Other salts are

phenyl-ethyl barbiturate,	(luminal, phenobarbital)
n-butyl-ethyl barbiturate,	(neonal)
di-allyl barbiturate,	(dial)
calcium ethyl-iso-propyl barbiturate,	(ipral)
allyl-iso-propyl barbiturate,	(somnifen, numal)
the same combined with amidopyrin,	(allonal)
iso-amyl-ethyl barbiturate,	(amytal)

the sodium salt of the same, (sodium amytal)
sodium second-butyl-bromallyl barbiturate, (pernocton)
sodium ethyl-l-methyl-butyl barbiturate, (nembutal)
also medinal, noctal, and proponal.

All of these salts of brabituric acid are powerful hypnotics with marked sedative and antispasmodic effects. They have little effect upon the heart action and do not damage the liver. The rate and volume of respiration is diminished. Peristalsis is not interfered with and normal labor is not affected. The barbiturates are slowly eliminated by the kidneys. They may show cumulative effects to which some patients are specially susceptible.

In large doses, barbiturates may cause a serious fall in blood pressure with symptoms of shock. The respiration is seriously depressed and bronchopneumonia or edema of the lungs may follow. Restlessness is followed by delirium and stupor. During recovery, there may be a long drawn out period of excitement, requiring forcible restraint. The results of overdosage are particularly dangerous in cases of hypertension where rapid fall of blood pressure simulates shock, in kidney disease where further interference with kidney function may be disastrous, and in pulmonary affections when respiratory depression must be avoided.

The barbiturates vary in solubility, in rapidity of action and recovery, in rate of elimination and in cumulative effect. For use in anesthesia, sodium amytal is at present the most popular of these drugs.

Sodium amytal is a white, colorless powder with a pronounced bitter taste. At room temperature, one gram dissolves in two cc. of distilled water forming a colorless, clear, somewhat mucilaginous solution. Sodium amytal may be administered by mouth, by rectum, or intravenously. A concentrated solution, injected under the skin, has irritating effects and may produce sloughing of the tissues. Doses of .6 to 1. grams (10 to 15 grains) of sodium amytal in distilled water have been used by intravenous injection for production of complete anesthesia but are no longer recommended for this purpose. For administration by mouth, sodium amytal is available in capsules, each containing three grains of the drug, in which form it is an efficient pre-anesthetic hypnotic. To an adult patient, one capsule is administered on the evening before operation, to insure a quiet night's sleep. One to two hours before the time for operation, one to three capsules are given. The patient thus prepared, comes to the operating room in a quiet, sleepy condition and undergoes induction of general anesthesia without excitement or muscular spasm. Anesthesia is maintained with a reduced dosage of the

anesthetic agent. With nitrous oxide oxygen, the oxygen percentage may be more than 20 per cent., with ether, the dosage should be sharply reduced. Children under ten years of age take about one third the adult dose of sodium amytal. Pre-anesthetic use of sodium amytal produces little circulatory disturbance. The blood pressure may be slightly reduced and there is some respiratory depression. The sole precaution is to reduce the dosage of the general anesthetic below the customary level. The patients do not often suffer from nausea and vomiting following operation and have little or no recollection of circumstances connected with anesthesia or operation. In common with other barbiturates, administration of sodium amytal markedly diminishes the toxicity of regional anesthetics. This action results from the antispasmodic effect of the barbiturate in preventing the development of convulsions.

If administration of sodium amytal by mouth is undesirable, the same dose may be given by rectum as a suppository or enema.

Advantages of the pre-anesthetic use of sodium amytal:

Alleviation of the patient's pre-operative anxious state.

Lessened liability to excitement and respiratory spasm during induction of general anesthesia,

Reduced toxicity of regional agents,

Memory of anything connected with operation is fragmentary or absent,

Recovery is more comfortable.

Disadvantages of the use of sodium amytal:

Depression of respiration with possibility of difficulty during operation or of post-operative complication,

Occasional occurrence of excitement before or following anesthesia.

DeLee[14] reports: "Our recent experience with sodium amytal in painful labour has been disappointing, and several babies were born narcotized."

DERIVITIVES OF URETHANE

In animal experimentation, hedonal (methyl-propyl-carbinol urethane) has been used successfully as an anesthetic for intravenous injection.

OPIUM ALKALOIDS

MORPHINE

Morphine, the principal alkaloid of opium, has powerful hypnotic and analgetic powers, producing a specific depression of the sense of pain. The respiratory center is depressed, with resulting slow and shallow respiratory movements and the coughing reflex is diminished or abolished. The vomiting center is stimulated so that nausea and vomiting frequently follow the use of morphine. From stimulation of the oculomotor center, the pupil is contracted. The spinal reflexes are never stimulated but frequently are exaggerated. The heart action is stimulated and the frequency of the pulse is reduced. Peristalsis is diminished. Glandular secretions are checked and retention of urine is liable to occur. From depression of peristalsis and diminution of the intestinal secretions, constipation follows the use of morphine.

Depression of respiration and stimulation of the vomiting center and of the oculo-motor center due to morphine, may be antagonized by small doses of atropine. In some cases, morphine produces excitement instead of hypnosis. Gwathmey finds that a combination of magnesium sulphate with morphine has a hypnotic effect greater than would be expected from the combined effects of the drugs. By this synergistic action, the effects of morphine are intensified in degree and in duration.

Advantages of the pre-anesthetic use of morphine:

Apprehension of danger from the operation is reduced and the patient comes to the operating room in a quiet state of mind,

Lessened excitement during induction,

Relaxation more readily secured,

Less of the anesthetic required,

Diminished liability to development of shock,

Delayed recovery, with less post-operative discomfort.

Disadvantages of the pre-anesthetic use of morphine:

Respiratory depression, favoring development of pulmonary complications,

Depression of the coughing reflex, a safeguard against insufflation of deleterious matter,

Blocking secretions, especially kidney function.

HYOSCINE

Hyoscine, identical with scopolamin, is an alkaloid obtained from Hyoscyamus niger, a European plant. Hyoscine is a hypnotic and antispasmodic, depressing the cerebral cortex, the respiration, the heart action and the reflexes. A dose of one two-hundredth to one one-hundreth of a grain produces deep sleep. Larger doses produce a stage of excitement followed by delirium, with dilated pupils, slow shallow respiration and a slow, weak pulse. Combined with hyoscine, the effect of morphine is accentuated. The combination has been used for production of a form of semi-narcosis used in obstetrics and known as "twilight sleep." The effect is to reduce sensation and diminish the powers of attention without markedly interfering with the progress of labour. Because of the depressing effects of the drugs in the dosage required, this method has been found to be dangerous to both mother and child. Instances of idiosyncrasy to the effects of hyoscine are frequently encountered.

Hatcher[93], in a Report to the Council on Pharmacy and Chemistry of the American Medical Association, in 1910, reported that:

> The use of scopolamin and morphin alone, and unsupported by chloroform, ether or other anesthetic, is wholly unsuited for general anesthesia.
>
> Scopolamin and morphin are wholly unsuited in the present state of our knowledge, for use in general obstetric practice.

METHODS BY WHICH ANESTHETICS ARE ADMINISTERED

INHALATION

Every thirty seconds, the entire volume of the blood passes through the lungs. Spurred on by the contractions of the right heart, a part of this stream passes immediately to the nerve centers, where the changes necessary for the production of general anesthesia take place. By respiratory inhalation, general anesthesia can be rapidly induced and is under more accurate control than can be maintained by other methods.

The anesthetic gases must be administered free from admixture of atmospheric air and are usually inhaled from a closed rubber bag. If there is a check valve at the inspiratory opening, the patient constantly inhales fresh gas without rebreathing but if no such valve is in operation, he breathes to and fro into the bag. According to McKesson's principle of fractional rebreathing, when pressure is applied to the expira-

tory valve by a spring, the first part of each expiration, consisting of unused gas, passes back into the bag to be rebreathed, while the last part of the expiration, consisting of gas which has lost oxygen and acquired carbon dioxide in the depths of the lung, wastes through the expiratory valve as soon as the breathing bag becomes full. The proportion of rebreathing varies inversely to the rate of flow of fresh gas into the bag.

The vapors of the liquid anesthetics, requiring dilution with large proportions of atmospheric air, are administered by open methods. For the drop method, an evaporating surface, composed of several layers of gauze or stockinet, is held near the nose and mouth by a wire mask. The liquid anesthetic is applied drop by drop to the evaporating surface so that vapor may be drawn in with each inspiration. During expiration, a corresponding amount of vapor is wasted. The open cone is a funnel through which the patient breathes. In its distal end is fixed an evaporating surface upon which the liquid anesthetic is applied. With the open cone, the evaporating surface is at some distance from the patient's face, avoiding the chilling effect from evaporation of the liquid, evaporation is under control, and the small amount of rebreathing provided by the cone gives the added advantage of conserving carbon dioxide. The open cone is made from a newspaper covered with a towel. Permanent cones have been devised by Allis and by Blake. They lack the feature of cleanliness, present when a fresh cone is used for each case.

*The author's Gravitational Method of open anesthesia depends upon the specific gravity of the anesthetic agents. Gases and vapors which are heavier than air can be held in upright, open containers as can liquids, except for more rapid loss from diffusion. Heavy gases, introduced into a vertically placed cone which is closely fitted to the patient's face, sink to the bottom of the cone and are inspired with little admixture of atmospheric air. For this purpose, nitrous oxide with a specific gravity, 1.527, carbon dioxide, 1.977; ether vapor, 2.586; and oxygen, 1.1057, are available. For the gravimetric method, a cone is prepared from newspaper and covered with a towel. At one end of the cone, an evaporating chamber is arranged by fixing a diaphragm of gauze, held by an adjustable metal ring, two inches from the distal end of the cone. In the evaporating chamber is placed a wad of fluffed washed gauze to serve as the evaporating surface. If the cone is seven inches in height, a rebreathing space five inches deep is left below the evaporating chamber.

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*The paragraphs describing this method were omitted from the manuscript as originally submitted, lest their inclusion reveal the identity of the author.—W. P.

The proximal end of the cone is fitted closely to the patient's face. A¼ inch metal tube, five inches long, bent to a hair-pin curve and connected by rubber tubing to a gas-oxygen machine is hooked into the distal end of the cone. For the gas-oxygen sequence with this method, with the cone closely fitted to the patient's face, a flow of nitrous oxide at sixty to ninety gallons per hour is introduced through the tube, then oxygen with ten per cent. carbon dioxide is added until the patient shows signs of satisfactory gas oxygen anesthesia. Ether is next added to the evaporating surface from a measuring bottle. As the ether takes effect, the flow of nitrous oxide is diminished until the patient is inhaling a mixture of ether vapor, oxygen, carbon dioxide and atmospheric air. During the operation, ether is administered as indicated, sufficient flow of oxygen is maintained to keep the color perfectly normal, carbon dioxide is added when indicated, and nitrous oxide may be used to rapidly secure a deeper anesthetic zone. With an accurately measuring gas machine, no nitrous oxide need be wasted by this method. A slight flow of oxygen suffices to replace the oxygen displaced by the ether vapor. For ether anesthesia with no oxygen deprivation and no excess of carbon dioxide, somewhat more of the agent is required. A long series of cases of gas oxygen ether anesthesia by this method have resulted in some improvement in respect to postoperative nausea and vomiting, entire absence of postoperative pulmonary complications, and the enthusiastic approval of the patients. A few cases of nitrous oxide oxygen anesthesia without ether have been successfully conducted by this method.

Mechanical devices for vaporizing the liquid anesthetics have not succeeded in overcoming the advantages of constant, personal attention in inhalation anesthesia.

Advantages of inhalation methods of anesthesia:

Exact, minute to minute control of dosage,
Rapid response to changes in dosage,
Diminution of effect on the liver.

INSUFFLATION

Anesthetic gases or vapors may be introduced into the respiratory passages through a tube inserted through the mouth or nose into the oropharynx or down to the bifurcation of the trachea. Liquid anesthetics must first be vaporized and a proper mixture with air provided for insufflation. Mixtures of ether vapor with oxygen must be avoided as possibly explosive but chloroform with oxygen is free from this objection and has a remarkable record for safety. As the liquid from which

vaporization takes place constantly becomes colder, with a corresponding reduction in concentration of the vapor, some method of heating the liquid must be provided in order to maintain constant dosage.

Advantages of insufflation anesthesia:

For operations about the face and upper air passages, the face is free from anesthetic apparatus except for the nasal or oral tube. This is an important feature in anesthesia for mastoid operations, where the face should be free for inspection in order that irritation of the facial nerve may be detected.

In the prone posture, when heavy anesthetic gases or vapors tend to waste as they sink to the floor, insufflation places them effectively within the respiratory passages.

ORAL METHODS

An ether cocktail; ether, four fluidrams, liquid petrolatum, four fluidrams, peppermint water, five minims; provides a comfortable method for inducing anesthesia. The cocktail should be preceded and followed by a drink of port wine.

Morphine is administered by mouth but is slow in effect and interferes with digestion when so used.

The soluble barbiturates are preferably administered by mouth.

RECTAL ANESTHESIA

The solution for ether-oil colonic anesthesia is composed of ether, 120. to 180. cc., liquid petrolatum, 60. to 90. cc., and paraldehyde, 8. cc. This mixture, thoroughly shaken and warmed, is slowly administered as an enema. The ether is gradually absorbed and anesthesia persists for several hours.

The solution of avertine is administered by rectum.

When oral administration is contraindicated, the soluble barbiturates may be administered as enema or suppository with complete satisfaction.

Advantages of rectal anesthesia:

Anesthesia may be induced without the knowledge or cooperation of the patient. This feature is invaluable in work among the insane.

Administration may be intrusted to a nurse, without the presence of a trained anesthetist.

Disadvantages of rectal methods:

Greater toxic effect on the liver,
Lack of immediate control of dosage.

INTRAVENOUS ANESTHESIA

Chloral was the first drug recommended for intravenous anesthesia. Ten years ago, a five to seven and one half per cent. solution of ether in sterile saline or Ringer's solution was extensively used for intravenous general anesthesia. More recently, a solution of soluble barbiturate has been utilized.

The intravenous route offers no advantages over other, safer methods.

HYPODERMATIC GENERAL ANESTHESIA

A subcutaneous injection of 1/200 to 1/50 grain, (.3 to 1.2 milligrams) of scopolamine with 1/6 to 1/3 grain, (1 to 2 centigrams) morphine produces partial anesthesia with loss of consciousness. This method of "twilight sleep" has been used in obstetrics but is inherently dangerous to the mother and still more to the child.

REGIONAL METHODS

INFILTRATION

Subcutaneous injection of the solution of a regional anesthetic causes a localized paralysis of the sensory nerve endings. The solution is so injected as to form a successive series of wheals, each representing an area of local anesthesia which may be incised without perception of pain, after which the subjacent tissues may in turn be injected. In Schleich's edematization method, large quantities of a dilute solution are injected diffusely, without regard to the location of the nerve supply.

CONDUCTION ANESTHESIA OR NERVE BLOCK

In the endoneural method, the agent is injected within the sheath of a large nerve, producing anesthesia of the entire region supplied by the nerve. The effect is produced almost instantly.

By perineural injection, the anesthetic is placed as closely as possible to the nerve trunk, depending upon diffusion to bring it into contact with the nerve fibers.

In plexus block, the anesthetic is injected around a nerve plexus and affects the distribution of the plexus. The brachial plexus is thus anesthetized by injection between the clavicle and the first rib.

For paravertebral anesthesia, the spinal nerves are blocked at their point of exit from the intervertebral foramina. When this method is successful, it provides satisfactory anesthesia for intra-thoracic and intra-abdominal operations. The scope of the method extends from the first intercostal to the fourth lumbar nerve.

Para-sacral anesthesia results from blocking the sacral nerves as they emerge from the anterior sacral foramina. The results are reliable but the technic is difficult.

For trans-sacral anesthesia, the nerves are blocked in the posterior sacral foramina. The method is safe and reliable and the technic simpler than in the para-sacral method.

Sacral anesthesia is also known as caudal, epidural, extradural, and intra-sacral anesthesia. A lumbar puncture needle is passed through the sacrococcygeal membrane into the sacral canal and through the needle, 30 to 50 cc. of 1 per cent. aqueous procaine solution is injected. Anesthesia is complete within twenty minutes and may last as long as two or three hours. The parts affected are the perineum and gluteal region, the anus and lower part of the rectum, the penis and urethra, the prostate and the vulva and vagina. Sacral anesthesia is valuable in obstetrics, as pain is relieved without interference with uterine contractions. The technic is simple and results in a safe and efficient regional anesthesia.

Advantages of these regional methods:

Consciousness is not lost,
It is not necessary to restrict the intake of food and liquid before and after operation,
Lack of respiratory irritation,
Absence of interference with functions of the liver, kidneys and of peristalsis,
Absence of post-operative alimentary disturbance.

Disadvantages of regional methods:

Mental worry and strain on the part of the patient,
Activity of the reflexes in intra-abdominal work,
Danger from toxic effects of the drugs employed,
Danger of spreading infection,
Lack of efficiency except with highly developed technic.

Spinal anesthesia is also known as lumbar anesthesia, rachianesthesia, intraspinal block, and subarachnoid block. The adult spinal cord reaches downwards as far as the lower body of the first lumbar

vertebra. The spinal cord is invested with three membranes; the pia mater, closely adherent to the cord; the arachnoid, separated from the pia mater by a considerable interval which is called the subarachnoidean space; and the dura mater, lying in close apposition to the bones of the spinal canal. The subarachnoidean space is completely filled with serous fluid, the cerebro-spinal fluid, which has a specific gravity of 1.007 and is normally under a positive pressure of 60 to 120 mm. of water. The scope for spinal anesthesia extends from the second to the fifth lumbar interspace. Of the various drugs and methods of administration, neocaine dissolved in spinal fluid is the most popular. The spinal puncture needle is 20 G., 3½ inches long. Under the strictest antiseptic precautions, this needle is introduced into the subarachnoidean space and one or two cc. of spinal fluid is withdrawn in which to dissolve the anesthetic. The anesthetic solution is injected and is mixed with spinal fluid by withdrawing and reinjecting the mixture. As the anesthetic solution is slightly heavier than spinal fluid, the direction of diffusion may be somewhat controlled by the posture of the patient immediately following the injection. The intra-spinal dose of neocaine is .01 gm. (.14 grain) for each fifteen pounds of body weight, with .12 gm. as the maximum individual dose. The extent of the anesthesia depends upon the amount of drug injected, the amount of spinal fluid withdrawn and reinjected, the lumbar space chosen for injection, the force with which the injection is made, and the posture of the patient during the period immediately following the injection. The perineum and feet are first anesthetized, then anesthesia rapidly spreads up the lower limbs and body to reach its upper limit. The upper safe limit is at the costal margin. Anesthesia reaches its maximum intensity within fifteen minutes. The average duration of high anesthesia is thirty to sixty minutes and of low anesthesia is forty-five to ninety minutes.

Advantages of spinal anesthesia:

The technic is simple and easily applied,
Consciousness is not lost,
It is not necessary to restrict the intake of food and liquid before and after the operation,
Complete muscular relaxation,
Peristalisis is stimulated, not depressed,
Lack of respiratory irritation,
The normal functions of the liver, kidneys, and intestines are not disturbed,
Post-operative discomfort is minimized.

Disadvantages of spinal anesthesia:

Mental worry and strain on the part of some patients,
Limited field of application,
Limited duration of anesthesia,
Occurrence of severe, persistent headaches,
Liability to ocular paralysis or to meningeal infection,
Danger from breaking needles or from injury to the nerves of the cauda equina,
The fall in blood pressure, which frequently is serious and sometimes fatal.

LOCAL ANESTHESIA BY EXTERNAL APPLICATION TO MUCOUS MEMBRANES

During some nasal operations, ten times the fatal dose of cocaine has been used by external application without serious results. Ten times the fatal dose of alypin has been injected into the bladder, often without noticeable reaction. The safety of these doses depends upon an unbroken mucous membrane. If the application follows traumatization of the mucous membrane so that the drugs gain rapid entrance to the circulation, severe, sometimes fatal, reactions may result.

STATISTICS

The simplest method for determining the relative danger from the various anesthetics would seem to be the collection of results from the records of hospitals and municipal bureaus. These statistics, however, are often disappointing. Many of the deaths which occur under anesthesia are never reported in available form. If we could learn the entire list of anesthetic fatalities, we would still lack an accurate estimate of the entire number of administrations. From lack of a standard as to what constitutes death from an anesthetic, comparative statistics of the safety of anesthetics are often misleading. While statistics are subject to the elements of inaccuracy noted, a collection of great numbers of such figures is of value in determining the comparative safety of the anesthetic agents.

Gwathmey[1] obtained from 386 American hospitals records of 488,866 cases of anesthesia with 111 deaths, a mortality of 1 in 4,404. Among the different agents were:

	CASES	DEATHS	RATE
Ether	294,653	65	1 in 4,533
Nitrous oxide ether	64,242	10	1 in 6,424
Local anesthesia	30,846	0	
Chloroform	22,513	14	1 in 1,608
Chloroform ether	22,015	2	1 in 10,007
Ethyl chloride	12,261	0	
Nitrous oxide oxygen	11,087	0	

Miller[2] compiled from literature, series of cases reported from personal observation or intimate knowledge of the observers.

He found:

	CASES	DEATHS	RATE
Chloroform	1,034,025	392	1 in 2,665
Ether	865,162	108	1 in 8,010
Ethyl chloride	83,750	8	1 in 10,470
Nitrous oxide oxygen	80,483	2	1 in 40,241
Scopolamine morphine	39,308	59	1 in 666
Spinal anesthesia	34,747	56	1 in 620

NITROUS OXIDE

Teter[3] collected 938,924 cases under nitrous oxide alone, 32,172 cases with air, and 190,724 cases with oxygen:

	CASES	DEATHS	RATE
Nitrous oxide	1,161,820	2	1 in 580,710

McKesson[4], from replies to a questionnaire from one hundred and thirty exodontists, found:

	CASES	DEATHS	RATE
Nitrous oxide oxygen	500,000	41	1 in 12,195

Baldwin[5] thinks that nitrous oxide oxygen is the most dangerous anesthetic and reports fourteen deaths, and later six in addition, under its influence in the vicinity of Cleveland, Ohio.

McCormick[6] collected seventy-nine deaths under nitrous oxide oxygen and, by including results from other observers, finds that 163 deaths have occurred in the United States.

ETHYLENE

Salzer[7], from a questionnaire sent to 478 hospitals in the United states, found:

	CASES	DEATHS	RATE
Ethylene	332,721	1	1 in 332,721

Among the 332,721 cases, there were ten explosions, three with minor injuries, and one death.

Landry[72] reported three deaths due to ethylene.

Henderson[8], from replies from fifty-eight surgeons to a questionnaire of W. J. M. Scott, reported:

	CASES	EXPLOSIONS	DEATHS
Ethylene	163,000	18	1

Of these explosions, three were serious and one fatal.

Ethylene explosions have been reported by:

	NUMBER OF EXPLOSIONS
Davis[9]	1
Lundy[10]	1
Heaney[12]	2
Herb[13]	5
McKesson[14]	1
Siebald[15]	2
Lillies[16]	1
Peterson[17]	1
Henderson[18]	24 6 serious . 3 fatal.

ETHER

Keen[19] collected statistics of etherization from sixty-seven members of the American Surgical Association. In twenty replies, the figures were exact and showed:

	CASES	DEATHS	RATE
Ether	262,002	34	1 in 7,706

In the other forty-seven replies, the number of cases and of deaths were estimated:

	CASES	DEATHS	RATE
Ether	365,500	73	1 in 4,884

REGIONAL

Committees of the American Medical Association have collected reports of one-hundred and five fatalities under local anesthetics in eye, nose and throat operations:

	AGENTS	FATALITIES
Mayer[20], 1920	cocaine	14
	procaine	6
Mayer[21], 1921	cocaine	11
	cocaine and procaine	5
	procaine	3
	apothesine and cocaine	1
	apothesine	1
	alypin and cocaine	1
	agent not reported	5
Mayer[22], 1924	alypin	1
	apothesine	4
	butyn	4
	butyn and cocaine	1
	cocaine alone or with procaine	26
	procaine	2
	stovaine	1
	unclassified	2
	due to other causes than local anesthetic	2
		2
Bulson[23] 1925	cocaine	2
	procaine	1
Mayer[24], 1928	butyn	1
	cocaine alone or with procaine	5
	procaine	8
Total of these series:		
	alypin	1
	apothesine	5
	butyn	5
	cocaine alone or in combination	66
	procaine	20
	stovaine	1
	unclassified	7
	total	105

Watson-Williams[25] collected fifty deaths from cocaine and five from butyn. Other deaths from local anesthetics have been reported by:

	AGENTS	FATALITIES
Flemming[26]		6
Miller[27]	alypin	3
Orr[28]	B eucaine	1
Spencer[29]	quinine hydrochloride	1
Moller[30]	cocaine	1
Shoemaker[31]	procaine	1
Hering[32]		3
Shurley[33]	procaine	1
Babcock[34]	cocaine	1
Martin[35]	procaine	1
Snapp[36]	procaine	1
Thompson[37]	procaine	1
Klotz[38]	cocaine	102
	other agents	49
Proskauer[39]	alypin	1
Lichtenstein[40]	alypin	1

These three-hundred and thirty-five deaths which have been reported as due to local anesthetics, are only a portion of all that undoubtedly have occurred. The entire number is very small when compared with the tremendous number of administrations.

SPINAL ANESTHESIA

The following series of cases of spinal anesthesia were collected from literature:

REPORTER	CASES	DEATHS	RATE
Strauss[41]	32,717	46	1 in 755
Chiene[42]	12,000	22	1 in 545
Violet and Fisher[43]	30,000	36	1 in 833
Rygh and Bessesen[94]	250,895	75	1 in 3,345

In addition to the 34,747 cases of spinal anesthesia collected by Miller[2], the following series have also been reported:

REPORTER	CASES	DEATHS
LeFilliatre[44]	194	0
Gellhorn[35]	169	0
Stanley[45]	280	0
Knight[46]	305	0
Weston[47]	170	0
Yount[48]	7,000	2
Blanc[49]	200	1
Achard[50]	413	0
Delmas[51]	600	0
Duboff[52]	12	1
Meriel and LeFebvre[53]	1,000	0
Chute[96]	328	0
Steel[54]	5,000	3
Babcock[62]	5,000	10
Babcock[62], later series	10,000	0
Martin and Arbuthnot[55]	6,000	2
Campbell[56]	536	2
Ducuing[97]	6,000	3
Morrison[57]	11,000	0
Holder[58]	151	0
Case[98]	1,100	0
Sise[99]	950	1
Rapaport[59]	500	0
McCormack[60]	4,000	0
Jackson[61]	1,000	0
Miller[2]	34,747	56
Total	96,655	81

The rate of mortality from this series of 96,655 cases of spinal anesthesia is 1 in 1,193. The figures show better results in recent cases than in those formerly reported. Babcock[62], from his experience with 15,000 cases, places the mortality at 1 in 10,000 in selected cases, but 1 in 500 in unselected cases including the bad surgical risks.

AVERTINE

A committee of the Northwest German Surgical Society[63] places the mortality from avertine at 1 in 7,500. Other observers find:

REPORTER	CASES	DEATHS	RATE
Glaesmer and Amersbach[63]	3,000	13	1 in 231
Waters and Muehlberger[64]	234	1	1 in 234
Blomfield and Shipway[65]	198	2	1 in 99

Avertine deaths have been reported by MacWilliams and Wilson[67] and by Kallman[66].

SODIUM AMYTAL

Series of cases using sodium amytal have been reported by:

REPORTER	CASES	DEATHS
Zerfas and McCullum[68]	800	0
Lundy[69]	457	0
Link[70]	47	0

A death from pernocton was reported by Eichelter[71]. Flemming[23] reported two deaths from hedonal.

SCOPOLAMINE

The following series of cases of morphine-scopolamine anesthesia have been reported:

REPORTER	CASES	DEATHS	RATE
Wood[72]	1,988	9	1 in 221
Maass[73]	1,499	11	
Roith[74]	4,000	18	
Muhsam[75]	28,809	5	
Viron and Morel[76]	2,000	25	
Beach[77]	1,000	0	
Rongy[78]	2,000	0	
Total	41,296	68	1 in 607

An additional death was reported by Levy[79] and two by Flemming[26].

POST-OPERATIVE PULMONARY COMPLICATIONS

Homans[80] compared the death rate from pulmonary complications following laparotomy in German hospitals and in hospitals of Boston:

	CASES	MORTALITY
German hospitals	15,043	4.4%
Boston hospitals	3,089	.4%

Occurrence of post-operative pulmonary complications:

OBSERVER	CASES	COMPLICATIONS
Beckman[81]	6,825	87 1.3 %
Bancroft[82]	1,413	15 1. %
		7 deaths .5 %
McKesson[83]	39,438	3.03%
Cleveland[84]	1,940	65 3.3 %
		7 deaths .35%
Cutler and Hunt [85]	18,075 laparotomies	4.5 %
Mandl[86]	1,379 laparotomies	14.5 %
	1,585 other operations	8.5 %

Comparison of pulmonary complications following different anesthetics:

REPORTER	ANESTHETIC	CASES	COMPLICATIONS
Davis[87]	general	1,500 hernia	130 8.6 %
	local	170 hernia	25 15. %
Whipple[88]	ether		2.8 %
	gas-oxygen		1.6 %
	local		3.1 %
Sise[89]	ether		3.1 %
	gas-oxygen		1.8 %
	local		7.5 %
Miller[100]	gas-ether	3,501	33 .94%
			6 deaths .17%
	gas-oxygen	1,493	19 1.2 %
			4 deaths .26%
Rapaport[59]	spinal	500	19 3.8 %
			7 deaths 1.4 %
Campbell[56]	gas-oxygen		5. %
	spinal		.7 %
Lundy[11]	ethylene-ether	600 upper abdominal	53 8.8 %
	ether	600 upper abdominal	59 9.8 %
	with preliminary morphine	465	47 10. %
	without preliminary medication	728	65 9.8 %

EFFICIENCY OF REGIONAL ANESTHESIA

OBSERVER	CASES	RESULT
McCuskey[91]	8,027	86.3 per cent. satisfactory 13.7 per cent. unsatisfactory 7. per cent. failure 5.9 per cent. fair .8 per cent. poor 1.8 per cent. marked reaction 3.5 per cent. slight reaction
Henline[92]	1,000	80.5 per cent. satisfactory 13.5 per cent. fair 5.9 per cent. poor

EFFICIENCY OF SPINAL ANESTHESIA

OBSERVER	CASES	RESULT
Rankin & McCuskey[90]	325	necessary to resort to general anesthesia in 12 per cent.
Chute[96]	328	necessary to resort to general anesthesia in 8 per cent.

CONCLUSIONS

In the preceding pages, an answer is given to the question of the values and dangers of the anesthetic agents. The answer will have different interpretations depending upon personal experience and training. If we knew but one of the anesthetic agents, this one would be considered a priceless boon and would be extensively used, whatever its inefficiency and danger. A like condition can be found at the present time in many institutions and communities where one routine anesthetic; ether, nitrous oxide, ethylene, regional, or spinal anesthesia, is used to the exclusion of others. Opinions change also from time to time, as in the case of intravenous etherization, which ten years ago, promised to displace all other methods, but today, is unheard of. The only method which has stood the test of time is ether inhalation, which since its introduction by Morton, has never failed to be utilized for overcoming the shortcomings of other methods. Ether inhalation occupies the position of the most extensively used method of anesthesia in spite of great handicaps. Millions of dollars have been invested in accurate measuring apparatus for use with nitrous oxide and ethylene. For regional and spinal anesthesia, a highly developed technic is available. Except for the continuous process devised by Squibb for manufacture of the agent, the work of Boothby and of Connell on measured dosage, the oil-ether colonic method of Gwathmey, and the introduction of insufflation, no noteworthy improvement over Morton's method has been made since its origin, eighty-five years ago.

The value of an anesthetic depends upon its safety, its efficiency, and the degree of comfort afforded the patient. Chloroform is probably the most efficient anesthetic but its immediate toxic action on the heart and its delayed poisonous effect put it on the danger list. Ethyl chloride provides an ideal induction to less agreeable anesthetics but is inferior to nitrous oxide in safety.

Statistics of long series of successful nitrous oxide oxygen administrations prove the safety of this anesthetic in properly selected cases. That nitrous oxide oxygen is not an efficient anesthetic is frequently indicated by absence of muscular relaxation and persistence of active reflexes. Attempts to secure satisfactory anesthesia in spite of these elements of inefficiency have resulted in many fatalities, due not to inherent danger from the agent but to abuse of its limited powers. The efficiency of nitrous oxide oxygen can be increased by proper preliminary medication and by the addition of regional anesthesia. With preliminary administration of soluble barbiturates and morphine and with intelligent use of novocaine during operation, even difficult rectal opera-

tions may be performed safely and with satisfaction under nitrous oxide oxygen.

Ethylene oxygen compares with nitrous oxide oxygen in intrinsic safety and is much more efficient. The chance of explosion of mixtures of ethylene and oxygen acts as deterrent to its more extensive use. It is not the number but the nature of these explosions which is considered. One who would pass away quietly in bed without protest, revolts at the idea of violent death from intra-pulmonary explosion.

In selected cases, regional anesthesia is invaluable. Regional anesthesia is not entirely efficient, but this factor is subject to great variation, depending upon the skill of the administrator. Consciousness of the patient during operation is generally of advantage but some individuals of nervous disposition may be seriously affected by the resulting nervous worry and strain. The number of deaths which have resulted from regional anesthesia is small in comparison to the total number of administrations but is sufficient to indicate the inherent danger of the method. A combination of regional with general anesthesia is often of great value in operations for which both unconsciousness and muscular relaxation are desired, a small dose of the general anesthetic rendering the patient unconscious while the regional agent is relied upon to produce relaxation.

The efficiency of spinal anesthesia is limited in extent and in duration. As with regional anesthesia, the preservation of consciousness is of advantage with some patients and an objection to others. The technic is simple. Muscular relaxation is the most perfect attained by any anesthetic, so that abdominal operations may be done more quickly, compensating to a considerable extent for the inefficiency of the method as to duration. When the time limit of spinal anesthesia is overstepped by the length of the operation, a general anesthetic is used to prolong anesthesia. It is questionable whether general anesthesia throughout, supplemented by regional anesthesia to secure relaxation, would not be preferable. Statistics show remarkable gains in the safety of spinal anesthesia in recent years, doubtless due to the introduction of the less toxic agent, novocaine or neocaine. It is still possible to find reports of one death to 100 cases.

The hypnotic drugs, in overdosage, produce pronounced respiratory depression and are not suitable agents for production of complete anesthesia. For preliminary preparation for general or regional anesthesia, they are of great value.

For operations about the face and upper air passages, insufflation is invaluable.

In obstetrics, the anesthetic must be carefully chosen. Respiratory depression of the new-born child and additional burden for the already overtaxed kidneys of the mother must be avoided.

ANESTHETICS ARRANGED IN ORDER OF THEIR COMPARATIVE VALUE UNDER DIFFERENT CONDITIONS

For abdominal operations:
- Gas-oxygen or ether with regional anesthesia
- Ether inhalation
- Spinal anesthesia

For thoracic operations:
- Gas-oxygen under positive pressure
- Regional anesthesia

For rectal or perineal operations:
- Gas-oxygen or ether with regional anesthesia
- Ether inhalation
- Regional anesthesia
- Spinal anesthesia

For operations on the extremities:
- Regional anesthesia
- Gas-oxygen
- Ether inhalation

For operations on the face or upper air passages:
- Ether insufflation
- Regional anesthesia

In obstetrics:
- Gas-oxygen
- Ether inhalation
- Ether oil colonic anesthesia
- Sacral anesthesia

With renal disease:
- Regional anesthesia
- Gas-oxygen
- Spinal anesthesia

With pulmonary disease:
- Regional anesthesia
- Spinal anesthesia
- Gas-oxygen

For induction of general anesthesia:
- Gas-oxygen

For preliminary preparation:
- Morphine hypodermatically
- Soluble barbiturate by mouth or rectum

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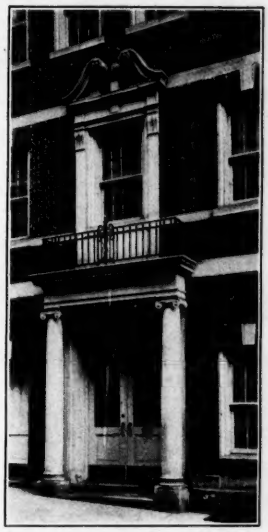

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